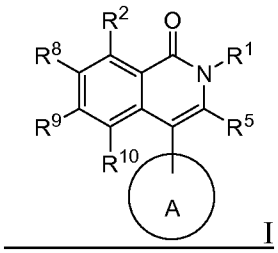
Amendments to the Claims

Claims 1-6 (cancelled)

Claim 7 (Currently Amended)

A compound of the structure:



I

or a pharmaceutically acceptable salt, crystal form, or hydrate, wherein:

A is

a) an aryl ring, wherein any stable aryl ring atom is independently unsubstituted or substituted with

1) halogen,

2) NO_2,

3) CN,

4) $CR^{46}=C(R^{47}R^{48})_2$,

5) $C\equiv C\ R^{46}$,

6) $(CR^iR^j)_rOR^{46}$,

7) $(CR^iR^j)_rN(R^{46}R^{47})$,

8) $(CR^iR^j)_r\ C(O)R^{46}$,

9) $(CR^iR^j)_r\ C(O)OR^{46}$,

10) $(CR^iR^j)_rR^{46}$,

11) $(CR^iR^j)_r\ S(O)_{0-2}R^{61}$,

12) $(CR^iR^j)_r\ S(O)_{0-2}N(R^{46}R^{47})$,

13) $OS(O)_{0-2}R^{61}$,

14) $N(R^{46})C(O)R^{47}$,

15) $N(R^{46})S(O)_{0-2}R^{61}$,

16) $(CR^iR^j)_rN(R^{46})R^{61}$,

17) $(CR^iR^j)_rN(R^{46})R^{61}OR^{47}$,

18) $(CR^iR^j)_rN(R^{46})(CR^kR^l)_SC(O)N(R^{47}R^{48})$,
19) $N(R^{46})(CR^iR^j)_rR^{61}$,
20) $N(R^{46})(CR^iR^j)_rN(R^{47}R^{48})$,
21) $(CR^iR^j)_rC(O)N(R^{47}R^{48})$, or
22) oxo, or

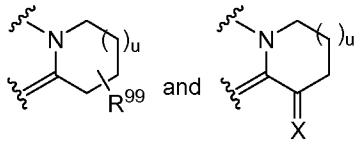
b) a heteroaryl ring selected from the group consisting of
a 5-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting or N, O or S,
a 6-membered unsaturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and
a 9- or 10-membered unsaturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting or N, O or S;

wherein any stable S heteroaryl ring atom is unsubstituted or mono- or di-substituted with oxo, and any stable C or N heteroaryl ring atom is independently unsubstituted or substituted with
1) halogen,
2) NO_2,
3) CN,
4) $CR^{46}=C(R^{47}R^{48})_2$,
5) $C\equiv CR^{46}$,
6) $(CR^iR^j)_rOR^{46}$,
7) $(CR^iR^j)_rN(R^{46}R^{47})$,
8) $(CR^iR^j)_r C(O)R^{46}$,
9) $(CR^iR^j)_r C(O)OR^{46}$,
10) $(CR^iR^j)_rR^{46}$,
11) $(CR^iR^j)_r S(O)_{0-2}R^{61}$,
12) $(CR^iR^j)_r S(O)_{0-2}N(R^{46}R^{47})$,
13) $OS(O)_{0-2}R^{61}$,
14) $N(R^{46})C(O)R^{47}$,
15) $N(R^{46})S(O)_{0-2}R^{61}$,
16) $(CR^iR^j)_rN(R^{46})R^{61}$,
17) $(CR^iR^j)_rN(R^{46})R^{61}OR^{47}$,
18) $(CR^iR^j)_rN(R^{46})(CR^kR^l)_SC(O)N(R^{47}R^{48})$,
19) $N(R^{46})(CR^iR^j)_rR^{61}$,
20) $N(R^{46})(CR^iR^j)_rN(R^{47}R^{48})$,

21) $(CR^iR^j)_rC(O)N(R^{47}R^{48})$, or

22) oxo;

R^1 and R^5 together with the atoms to which they are attached, form a ring selected from the group of structures consisting of



where u is 0 or 1, R^{99} is hydrogen or -OH, and X is O or ξ=NOH;

R^2, R^8, R^9 and R^{10} are independently selected from:

1) hydrogen,

2) halogen,

3) NO_2,

4) CN,

5) $CR^{43}=C(R^{44}R^{45})$,

6) $C\equiv CR^{43}$,

7) $(CR^eR^f)_pOR^{43}$,

8) $(CR^eR^f)_pN(R^{43}R^{44})$,

9) $(CR^eR^f)_pC(O)R^{43}$,

10) $(CR^eR^f)_pC(O)OR^{43}$,

11) $(CR^eR^f)_pR^{43}$,

12) $(CR^eR^f)_pS(O)_{0-2}R^{60}$,

13) $(CR^eR^f)_pS(O)_{0-2}N(R^{43}R^{44})$,

14) $OS(O)_{0-2}R^{60}$,

15) $N(R^{43})C(O)R^{44}$,

16) $N(R^{43})S(O)_{0-2}R^{60}$,

17) $(CR^eR^f)_pN(R^{43})R^{60}$,

18) $(CR^eR^f)_pN(R^{43})R^{60}OR^{44}$,

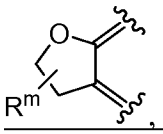
19) $(CR^eR^f)_pN(R^{43})(CR^gR^h)_qC(O)N(R^{44}R^{45})$,

20) $N(R^{43})(CR^eR^f)_pR^{60}$,

21) $N(R^{43})(CR^eR^f)_pN(R^{44}R^{45})$, and

22) $(CR^eR^f)_pC(O)N(R^{43}R^{44})$,

or R^2 and R^8 are independently as defined above, and R^9 and R^{10}, together with the atoms to which they are attached, form the ring


, where R^m is C_{1-6}alkyl;

R^a, R^b, R^c, R^d, R^e, R^f, R^g, R^h, R^i, R^j, R^k, and R^l are independently selected from the group consisting of:

1) hydrogen,
2) C_1-C_6 alkyl,
3) halogen,
4) aryl,
5) R^{80},
6) C_3-C_{10} cycloalkyl, and
7) OR^4,

said alkyl, aryl, and cycloalkyl being unsubstituted, monosubstituted with R^7, disubstituted with R^7 and R^{15}, trisubstituted with R^7, R^{15} and R^{16}, or tetrasubstituted with R^7, R^{15}, R^{16} and R^{17};

R^4, R^{40}, R^{41}, R^{42}, R^{43}, R^{44}, R^{45}, R^{46}, R^{47}, R^{48}, R^{49}, R^{50}, R^{51}, R^{52}, and R^{53} and are independently selected from the group consisting of

1) hydrogen,
2) C_1-C_6 alkyl,
3) C_3-C_{10} cycloalkyl,
4) aryl,
5) R^{81},
6) CF_3,
7) C_2-C_6 alkenyl, and
8) C_2-C_6 alkynyl,

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R^{18}, di-substituted with R^{18} and R^{19}, tri-substituted with R^{18}, R^{19} and R^{20}, or tetra-substituted with R^{18}, R^{19}, R^{20} and R^{21};

R^6, R^{60}, R^{61}, R^{62} and R^{63} are independently selected from the group consisting of

1) C_1-C_6 alkyl,
2) aryl,
3) R^{83}, and
4) C_3-C_{10} cycloalkyl;

said alkyl, aryl, and cycloalkyl is unsubstituted, mono-substituted with R^{26}, di-substituted with R^{26} and R^{27}, tri-substituted with R^{26}, R^{27} and R^{28}, or tetra-substituted with R^{26}, R^{27}, R^{28} and R^{29};

R^7, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, R^{28}, and R^{29} are independently selected from the group consisting of

1) C_1-C_6 alkyl,

2) halogen,

3) OR^{51},

4) CF_3,

5) aryl,

6) C_3-C_{10} cycloalkyl,

7) R^{84},

8) $S(O)_{0-2}N(R^{51}R^{52})$,

9) $C(O)OR^{51}$,

10) $C(O)R^{51}$,

11) CN,

12) $C(O)N(R^{51}R^{52})$,

13) $N(R^{51})C(O)R^{52}$,

14) $S(O)_{0-2}R^{63}$,

15) NO_2, and

16) $N(R^{51}R^{52})$;

R^{80}, R^{81}, R^{82}, R^{83} and R^{84} are independently selected from a group of unsubstituted or substituted heterocyclic rings consisting of a 4-6 membered unsaturated or saturated monocyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting N, O and S, and a 9- or 10-membered unsaturated or saturated bicyclic ring with 1, 2, 3 or 4 heteroatom ring atoms selected from the group consisting or N, O or S; and

n, p, q, r, and s are independently 0, 1, 2, 3, 4, 5 or 6;

provided that

when R^9 is OCH_3, R^1 is CH_3 and R^5 is $C(CH_3)_3$, then A is substituted,

when R^9 is hydrogen, R^1 is CH_3, and R^5 is hydrogen, then A is substituted,

when R^9 is hydrogen, R^1 is CH_3, and R^5 is $C(CH_3)_3$, then A is substituted, provided the substituent is not CH_3, and

when R^9 is OCH_3, R^1 is CH_3, R^5 is CH_3, then A is substituted;

~~A compound of Claim 6,~~ wherein the compound, or a pharmaceutically acceptable salt thereof, is selected from the group consisting of

3-tert-butyl-4-(3-fluorophenyl)-6-methoxy-2-methylisoquinolin-1(2H)-one,

3-tert-butyl-4-(4-fluorophenyl)-6-methoxy-2-methylisoquinolin-1(2H)-one,

6-methoxy-2-methyl-4-phenylisoquinolin-1(2H)-one,

4-(3-fluorophenyl)-6-methoxy-2,3-dimethylisoquinolin-1(2H)-one,

4-(4-fluorophenyl)-6-methoxy-2,3-dimethylisoquinolin-1(2H)-one,

(1E)-11-(3-fluorophenyl)-9-methoxy-3,4-dihydro-2H-pyrido[1,2-b]isoquinoline-1,6-dione 1-oxime,

3-tert-butyl-6-hydroxy-2-methyl-4-phenylisoquinolin-1(2H)-one,

2,3-dimethyl-4-phenylisoquinolin-1(2H)-one,

3-tert-butyl-2-ethyl-6-methoxy-4-phenylisoquinolin-1(2H)-one,

3-tert-butyl-6-methoxy-4-phenylisoquinolin-1(2H)-one,

2-ethyl-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

6-methoxy-2-(2-methoxyethyl)-3-methyl-4-phenylisoquinolin-1(2H)-one,

2-(2-aminoethyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

2-(3-aminopropyl)-6-methoxy-3-methyl-4-phenylisoquinolin-1(2H)-one,

3-tert-butyl-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-6-carbonitrile,

3-tert-butyl-8-hydroxy-2-methyl-4-phenylisoquinolin-1(2H)-one,

3-tert-butyl-2-methyl-1-oxo-4-phenyl-1,2-dihydroisoquinoline-6-carboxamide,

3-tert-butyl-2-methyl-4-phenyl-6-(4-phenylbutoxy)isoquinolin-1(2H)-one,

3-tert-butyl-2-methyl-4-phenyl-6-[(5-phenylpentyl)oxy]isoquinolin-1(2H)-one,

11-(3-fluorophenyl)-9-methoxy-3,4-dihydro-2H-pyrido[1,2-b]isoquinoline-1,6-dione,

(+/-)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-b]isoquinolin-6-one,

(1*S*)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-b]isoquinolin-6-one,

(1*R*)-11-(3-fluorophenyl)-1-hydroxy-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-b]isoquinolin-6-one, and

11-(3-fluorophenyl)-9-methoxy-1,2,3,4-tetrahydro-6H-pyrido[1,2-b]isoquinolin-6-one.

8. (Withdrawn) A method of treating a condition in a mammal, the treatment of which is effected or facilitated by $K_V1.5$ inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting $K_V1.5$.

9. (Withdrawn) A method of Claim 8, wherein the condition is cardiac arrythmia.

10. (Withdrawn) A method of Claim 9, wherein the cardiac arrythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

11. (Withdrawn) A method of Claim 10, wherein the cardiac arrythmia is atrial fibrillation.

12. (Withdrawn) A method of preventing a condition in a mammal, the prevention of which is effected or facilitated by $K_V1.5$ inhibition, which comprises administering a compound of Claim 1 in an amount that is effective at inhibiting $K_V1.5$.

13. (Withdrawn) A method of Claim 12, wherein the condition is cardiac arrythmia.

14. (Withdrawn) A method of Claim 13, wherein the cardiac arrythmia is selected from the group consisting of atrial flutter, atrial arrhythmia and supraventricular tachycardia.

15. (Withdrawn) A method of Claim 14, wherein the cardiac arrythmia is atrial fibrillation.

16. (Withdrawn) A method of Claim 12, wherein the condition is a thromboembolic event.

17. (Withdrawn) A method of Claim 16, wherein the thromboembolic event is a stroke.

18. (Withdrawn) A method of Claim 12, wherein the condition is congestive heart failure.

19. (Currently amended) A pharmaceutical formulation comprising a pharmaceutically acceptable carrier and the compound Claim ~~1~~ 7 or a pharmaceutically acceptable crystal form or hydrate thereof.

20. (Currently Amended) A pharmaceutical composition made by combining the compound of Claim ~~1~~ 7 and a pharmaceutically acceptable carrier.

21. (Withdrawn) A method of treating cardiac arrythmia comprising administering a compound of Claim 1 with a compound selected from one of the classes of compounds consisting of antiarrhythmic agents having Kv1.5 blocking activities, ACE inhibitors, angiotensin II antagonists, cardiac glycosides, L-type calcium channel blockers, T-type calcium channel blockers, selective and nonselective beta blockers, endothelin antagonists, thrombin inhibitors, aspirin, nonselective NSAIDs, warfarin, factor Xa inhibitors, low molecular weight heparin, unfractionated heparin, clopidogrel, ticlopidine, IIb/IIIa receptor antagonists, 5HT receptor antagonists, integrin receptor antagonists, thromboxane receptor antagonists, TAFI inhibitors and P2T receptor antagonists.

22. (Withdrawn) A method for inducing a condition of normal sinus rhythm in a patient having atrial fibrillation, which comprises treating the patient with a compound of Claim 1.

23. (Withdrawn) A method for treating tachycardia in a patient which comprises treating the patient with an antitachycardia device in combination with a compound of Claim 1.